Directing hepatic differentiation of embryonic stem cells with protein microarray-based co-cultures.

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Public Summary:

Scientific Abstract:
Embryonic stem cells hold considerable promise in tissue engineering and regenerative medicine as a source of tissue-specific cells. However, realizing this promise requires novel methods for guiding lineage-specific differentiation of stem cells. In this study, we developed a micropatterned co-culture platform for stimulating hepatic differentiation of mouse embryonic stem cells (mESCs). Studies of mESC and hepatic cell adhesion preferences revealed that mESCs required fibronectin for attachment, while hepatic cells (HepG2) preferred collagen (I) substrate and did not adhere to fibronectin. Printing columns of collagen (I) and fibronectin spots (300 microm diameter), followed by sequential seeding of the two cell types, allowed the positioning of clusters of mESCs adjacent to groups of hepatic cells within the same microarray. These micropatterned co-cultures were maintained for up to two weeks in hepatic differentiation media supplemented. To examine the differentiation, mESCs were selectively extracted from the co-culture using laser microdissection and analyzed using real-time reverse transcriptase (RT)-polymerase chain reaction (PCR). These analyses revealed that mESCs co-cultured with HepG2 cells showed a decrease in pluripotency gene expression concomitant with up-regulation of endodermal genes. In addition, the co-culture format induced a significant increase in the expression of liver genes compared to mESCs cultured alone. In conclusion, micropatterned co-cultures of mESCs and hepatic cells showed a significant promise in driving stem cell differentiation towards hepatic phenotype. In the future, this cell culture platform will be further enhanced to enable efficient conversion of mouse and human ESCs to hepatocytes.